Immunologic Therapy with Cadi-05 for the Treatment of Advanced Melanoma

Paul J. Mosca MD, PhD
Lehigh Valley Health Network

Suresh G. Nair MD
Lehigh Valley Health Network, suresh.nair@lvhn.org

Susan K. Ayre RN, MA
Lehigh Valley Health Network, Susan_K.Ayre@lvhn.org

Wenjing Shi RN, MS
Lehigh Valley Health Network

Sherrine Eid MPH
Lehigh Valley Health Network, Sherrine.Eid@lvhn.org

See next page for additional authors

Published In/Presented At

Mosca, P., Nair, S., Ayre, S., Shi, W., Eid, S., Amin, S., Desai, D., Drabick, J., Khamar, B., Sharma, A., Markovic, S., & Robertson, G. (2010). *Immunologic therapy with Cadi-05 for the treatment of advanced melanoma.*

Authors
Paul J. Mosca MD, PhD; Suresh G. Nair MD; Susan K. Ayre RN, MA; Wenjing Shi RN, MS; Sherrine Eid MPH; Shantu Amin PhD; Dhimant Desai PhD; Joseph J. Drabick MD, FACP; Bakulesh M. Khamar MD; Arati Sharma PhD; Svetomir N. Markovic MD; and Gavin P. Robertson PhD

Immunologic Therapy with Cadi-05 for the Treatment of Advanced Melanoma

Paul J. Mosca, MD, PhD,[1] Suresh G. Nair, MD,[1] Susan K. Ayre, RN, MA,[1] Wenjing Shi, RN, MS,[1] Sherrine Eid, MPH,[1] Shantu Amin, PhD,[2] Dhimant Desai, PhD,[2] Joseph J. Drabick, MD,[2] Bakulesh M. Khamar, MD,[3] Arati Sharma, PhD,[2] Svetomir N. Markovic, MD, PhD,[4] Gavin P. Robertson, PhD[2]

[1]Lehigh Valley Health Network, Allentown, Pennsylvania; [2]Penn State Cancer Institute, Hershey, Pennsylvania; [3]Cadila Pharmaceuticals, Ahmedabad, India; [4]Mayo Clinic, Rochester, Minnesota

Background

- Cadi-05 is a heat-killed mycobacterial preparation with immunomodulatory properties.
- As a Toll-like receptor agonist, Cadi-05 has been postulated to have antineoplastic activity.

Purpose

- The primary objective of this study was to evaluate the safety and toxicity of Cadi-05 monotherapy in the treatment of advanced melanoma patients.

Experimental Design

- 12 patients with stage IV melanoma and measurable disease were treated with one, two, or three 8-week cycles of intradermal Cadi-05.
- Patient demographics are represented in Table 1 and clinical characteristics in Table 2.
- Patients who tolerated treatment without severe adverse events and did not progress were eligible to receive a maximum of three cycles.
- Clinical and translational endpoints were assessed at baseline and after each cycle.

Table 1. **Demographics**

Demographics	N	%
Age, Years		
Median (range)	74 (32-86)	
Sex		
Male	7	58
Female	5	42

Table 2. **Clinical Characteristics**

Clinical Characteristic	N	%
Prior Therapy		
Radiation therapy	6	50
Chemotherapy/targeted therapy*	6	50
High-dose interleukin-2 (IL-2)	5	42
Resection/debulking	3	25
Interferon alpha	2	17
Amputation	1	8
Gamma knife	1	8
GM-CSF	1	8
Other therapies	3	25
No. of Metastatic Sites		
<3	1	8
3-5	9	75
6-10	1	8
>10	1	8

*Included one or more of the following agents: temozolomide, thalidomide, paclitaxel, carboplatin, sorafenib.

Results

- Ten of 12 patients enrolled completed at least one cycle of treatment; two patients who failed to complete a single cycle did so because of complications related to disease progression.
- One patient experienced grade 3 toxicity related to treatment; no other patients had grade 3 or higher toxicity.
- There were no objective clinical responses.
- Mixed responses were observed in some patients with regression of one or more lung lesions despite progression elsewhere (Fig. 1).
- One patient developed vitiligo of the treated extremity (Fig. 2). Median follow-up was 6.5 months. Mean survival was 11.9 months (95% [5.8,18.0]), and median survival was 6.7 months (95% [3.5,10]).
- Prolonged survival was noted in patients who underwent prior high dose IL-2 treatment (20.7 months 95% CI [10.225, 31.082] versus 5.6 months 95% CI [3.90, 7.38], p = 0.03) (Fig. 3).
- Seven evaluable patients exhibited a decrease in CD4+FoxP3+ regulatory T cell frequency following one cycle of treatment (Fig. 4).

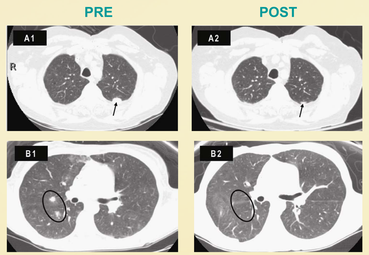

Figure 1. Two patients (A, B) experienced shrinkage of intrathoracic lesions during treatment. Patient B exhibited near-complete resolution of lung metastases despite progression in abdomen during one cycle of treatment.

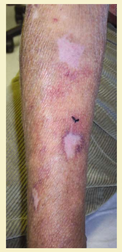

Figure 2. One patient developed vitiligo of the injected extremities. Although injections were administered into the upper arm, vitiligo developed in the forearm, thus representing a regional rather than local injection site phenomenon.

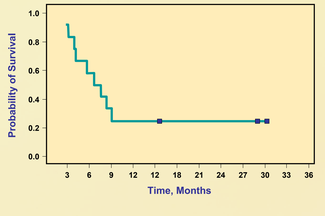

Figure 3. Kaplan-Meier curve representing all 12 patients in the study.

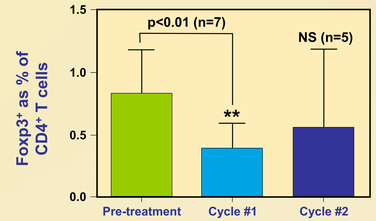

Figure 4. Immunologic effects of Cadi-05 on Tregs. Blood was collected from seven patients before (pre-treatment) and after first and second cycle of Cadi-05 treatment. PBMCs were stained with PE-Foxp3 after PeCy7-CD4. CD4+Foxp3+ cells were acquired and Foxp3+ as the percentage of CD4+ T cells was analyzed. Bars show mean ± SD. ** represents p < 0.01. NS, no statistical significance compared to both pretreatment and cycle 1.

Conclusions

- Cadi-05 is well tolerated in patients with advanced melanoma, but no objective responses were observed in this small single-arm study.
- Cadi-05 appears to decrease regulatory T cell frequency and thus may have desirable immunologic effects as an adjuvant agent in the treatment of advanced melanoma.

Supported by grants from the Dorothy Rider Pool Health Care Trust and the Penn State Cancer Institute.